IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

BANTICK et al

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February 14, 2002

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Please amend the above-identified application as follows:

IN THE CLAIMS

Please substitute the following amended claims for corresponding claims previously presented. A copy of the amended claims showing current revisions is attached.

3. (Amended) A compound of formula I, as defined in Claim 1-, wherein R^4 represents H or C_{1-6} alkyl when R^1 represents $-A^1C(O)N(R^4)R^5$.

4. (Amended) A compound of formula I, as defined in claim 1, wherein R^1 represents C_{1-6} alkyl or C_{4-6} cycloalkyl when R^1 represents $-A^1C(O)N(R^4)R^5$.

5. (Amended) A compound of formula I, as defined in claim 1, wherein R^4 and R^5 together represent pyrrolidinyl when R^1 represents $A^1C(O)N(R^4)R^5$.

6. (Amended) A compound of formula I, as defined in claim 2, wherein A^1 represents C_{1-3} alkylene, and R^4 represents H or C_{1-3} alkyl and R^5 represents C_{2-6} alkyl or C_{5-6} cycloalkyl, or R^4 and R^5 together represent pyrrolidinyl.

8. (Amended) A compound of formula I, as defined in Claim 1 , wherein R^4 represents C_{1-6} alkyl when R^1 represents $-A^1C(O)OR^4$.

9. (Amended) A compound of formula I, as defined in Claim 7 , wherein A^1 represents C_{1-5} alkylene and R^4 represents C_{1-4} alkyl.

11. (Amended) A compound as claimed in Claim 1 , wherein R^3 represents H, linear C_{1-10} alkyl, branched C_{3-10} alkyl, partially cyclic C_{4-10} alkyl, C_{4-10} cycloalkyl, optionally substituted linear C_{1-3} alkylphenyl, optionally substituted branched C_3 alkylphenyl.

13.. (Amended) A compound of formula I, as defined in claim 1, wherein R^2

represents OH.

14. (Amended) A compound of formula I, as defined in claim 1, wherein R^6 represents optionally substituted phenyl or C_{1-17} alkyl (which latter group may be linear or, when there are a sufficient number of carbon atoms, may be branched, be cyclic or partially cyclic, and/or be saturated or unsaturated) when R^2 represents $OC(O)R^6$..

17. (Amended) A compound of formula I, as defined in claim 1, wherein R^7 represents optionally substituted phenyl, C_{1-12} alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched, cyclic or partially cyclic, and/or saturated or unsaturated), or C_{1-3} alkylphenyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched) when R^2 represents $C(O)OR^7$.

20. (Amended) A compound of formula I, as defined in claim 1, wherein R^8 represents H or methyl, when R^2 represents $C(O)OCH(R^8)OC(O)R^9$.

21. (Amended) A compound of formula I, as defined in claim 1, wherein R^9 represents phenyl, or C_{1-8}, alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched and/or cyclic or partially cyclic) when R^2 represents $C(O)OCH(R^8)OC(O)R^9$.

22.. (Amended) A compound of formula I, as defined in claim 20 wherein R^8 represents H or methyl and R^9 represents phenyl, C_{5-7} cycloalkyl, linear C_{1-6} alkyl, branched C_{3-6} alkyl or partially cyclic C_{7-8} alkyl.

24. (Amended) A compound as claimed in claim 1 wherein, when R^1 represents R^3 and R^3 represents optionally substituted C_{1-3} alkylphenyl, the optional substituent C_{1-4} alkyl.

26. (Amended) A compound as claimed in claim 1 wherein, when R^2 represents $C(O)OR^7$ and R^7 represents optionally substituted C_{1-12} alkyl, the optional substituent is selected from halogen and C_{1-6} alkoxy..

28. (Amended) A compound as claimed in claim 1 wherein, when R^2 represents $C(O)OR^7$ and R^7 represents optionally substituted phenyl, the optional substituent is selected from C_{1-6} alkyl, C_{1-6} alkoxy and halogen..

30. (Amended) A compound as claimed in wherein when R^2 represents $C(O)OR^7$ and R^7 represents optionally substituted C_{1-3} alkylphenyl, the optional substituent is nitro.

39. (Amended) A pharmaceutical formulation including a compound of formula I

as defined in claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

40. (Amended) A compound of formula I, as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

41. (Amended) A compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of ·a condition where inhibition of thrombin is required..

42.. (Amended) A compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of thrombosis.

43. (Amended) A compound of formula I as defined in claim 1 , or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

44.. (Amended) The use of a compound of formula I as defined in claim 1 , or a pharmaceutically acceptable salt thereof as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

46. (Amended) The use of a compound of formula I as defined in claim 1 , or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of an

anticoagulant..

47. (Amended) A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

REMARKS

The above amendments have been made to place the application in a more traditional format. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made**."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

3. (Amended) A compound of formula I, as defined in Claim 1 [or Claim 2], wherein R^4 represents H or C_{1-6} alkyl when R^1 represents $-A^1C(O)N(R^4)R^5$.

4. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 3] claim 1, wherein R^1 represents C_{1-6} alkyl or C_{4-6} cycloalkyl when R^1 represents $-A^1C(O)N(R^4)R^5$.

5. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 3] claim 1, wherein R^4 and R^5 together represent pyrrolidinyl when R^1 represents $A^1C(O)N(R^4)R^5$.

6. (Amended) A compound of formula I, as defined in [any one of Claims 2 to 5] claim 2, wherein A^1 represents C_{1-3} alkylene, and R^4 represents H or C_{1-3} alkyl and R^5 represents C_{2-6} alkyl or C_{5-6} cycloalkyl, or R^4 and R^5 together represent pyrrolidinyl.

8. (Amended) A compound of formula I, as defined in Claim 1 [or Claim 7], wherein R^4 represents C_{1-6} alkyl when R^1 represents $-A^1C(O)OR^4$.

9. (Amended) A compound of formula I, as defined in Claim 7 [or Claim 8], wherein A^1 represents C_{1-5} alkylene and R^4 represents C_{1-4} alkyl.

11. (Amended) A compound as claimed in Claim 1 [or Claim 10], wherein R^3 represents H, linear C_{1-10} alkyl, branched C_{3-10} alkyl, partially cyclic C_{4-10} alkyl, C_{4-10} cycloalkyl, optionally substituted linear C_{1-3} alkylphenyl, optionally substituted branched C_3 alkylphenyl.

13.. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R^2 represents OH.

14. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R^6 represents optionally substituted phenyl or C_{1-17} alkyl (which latter group may be linear or, when there are a sufficient number of carbon atoms, may be branched, be cyclic or partially cyclic, and/or be saturated or unsaturated) when R^2 represents $OC(O)R^6$..

17. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R^7 represents optionally substituted phenyl, C_{1-12} alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched, cyclic or partially cyclic, and/or saturated or unsaturated), or C_{1-3} alkylphenyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched) when R^2 represents $C(O)OR^7$.

20. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R^8 represents H or methyl, when R^2 represents $C(O)OCH(R^8)OC(O)R^9$.

21. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12 or Claim 20] claim 1, wherein R^9 represents phenyl, or C_{1-8}, alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched and/or cyclic or partially cyclic) when R^2 represents $C(O)OCH(R^8)OC(O)R^9$.

22.. (Amended) A compound of formula I, as defined in [Claim 20 or Claim 21] claim 20 wherein R^8 represents H or methyl and R^9 represents phenyl, C_{5-7} cycloalkyl, linear C_{1-6} alkyl, branched C_{3-6} alkyl or partially cyclic C_{7-8} alkyl.

24. (Amended) A compound as claimed in [any one of the preceding claims] claim 1 wherein, when R^1 represents R^3 and R^3 represents optionally substituted C_{1-3} alkylphenyl, the optional substituent C_{1-4} alkyl.

26. (Amended) A compound as claimed in [any one of the preceding claims] claim 1 wherein, when R^2 represents $C(O)OR^7$ and R^7 represents optionally substituted C_{1-12} alkyl, the optional substituent is selected from halogen and C_{1-6} alkoxy..

28. (Amended) A compound as claimed in [any one of the preceding claims] claim 1 wherein, when R^2 represents $C(O)OR^7$ and R^7 represents optionally substituted phenyl, the optional substituent is selected from C_{1-6} alkyl, C_{1-6} alkoxy and halogen..

30. (Amended) A compound as claimed in [any one of the preceding claims] wherein when R^2 represents $C(O)OR^7$ and R^7 represents optionally substituted C_{1-3} alkylphenyl, the optional substituent is nitro.

39. (Amended) A pharmaceutical formulation including a compound of formula I as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

40. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

41. (Amended) A compound of formula I as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition where inhibition of thrombin is required..

42.. (Amended) A compound of formula I as defined in [any one of Claims 1 to

38] claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of thrombosis.

43. (Amended) A compound of formula I as defined in [any one of Claims 1 to 38] claim 1 , or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

44.. (Amended) The use of a compound of formula I as defined in [any one of Claims 1 to 38] claim 1 , or a pharmaceutically acceptable salt thereof as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

46. (Amended) The use of a compound of formula I as defined in [any one of Claims 1 to 38] claim 1 , or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of an anticoagulant..

47. (Amended) A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound of formula I as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.